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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,957	06/20/2003	Garth Powis	126387.530	6628

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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/600,957	POWIS, GARTH	
	Examiner	Art Unit	
	BRANDON J. FETTEROLF	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to the Amendment

The Amendment filed on 02/24/2005 in response to the previous Non-Final Office Action (10/20/2004) is acknowledged and has been entered.

Claims 7-30 are currently pending and under consideration.

Rejections Maintained, but amended in view of Applicants amendments:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7-18 remain rejected and new claims 19-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Oblong et al. (Cancer Chemotherapy and Pharmacology 1994; 34: 434-438, *IDS*) as evidenced by Chaplan et al. (US 5,849,737, 1998) and) and Padmanaban (US 20070105945, 2007).

Oblong et al. teach a composition comprising an agent in DMSO, wherein the agent acts as a reversible inhibitor of human thioredoxin (page 435, 1st column, *TR assay*, page 436, 1st column, 1st full paragraph and Title). With regards to the thioredoxin inhibitor, the reference teaches that the thioredoxin inhibitors are alkyl 2-imidazole disulfide analogues, such as 1-methylpropyl-2-imidazolyl disulfide (Title and page 435, 1st column, *Chemicals* and Fig. 1). Moreover, the reference teaches that the alkyl 2-imidazolyl disulfide analogues are useful at inhibiting cellular proliferation, e.g. cell growth (page 437, Fig. 4A,B and 2nd column, last paragraph). Thus, while Oblong et al. do not explicitly teach that the agent is useful in reducing or eliminating thioredoxin-associated apoptosis inhibition, the intended use of the compound must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A composition is a composition irrespective of what its intended use is. See In re Tuominen, 213

USPQ 89 (CCPA 1982). Secondly, although Oblong et al. does not explicitly teach that DMSO is an acceptable carrier for intravenous administration, the claimed limitation does not appear to result in a manipulative difference when compared to the prior arts disclosure because as evidenced by Chaplan et al., DMSO is an example of an acceptable carrier for intravenous administration (Example 1, lines 27-28). Similarly, although Oblong et al. does not explicitly teach that DMSO is an acceptable carrier for oral administration, the claimed limitation does not appear to result in a manipulative difference when compared to the prior arts disclose because as evidenced by Padmanaban et al., DMSO is an example of an acceptable carrier for oral administration (paragraph 0031). Thus the claimed composition appears to be the same as the prior art.

In response to this rejection, Applicants assert that the instant claims have been amended to include the limitation of "an acceptable carrier for intravenous administration" and new claims 19-30 include the limitation of "an acceptable carrier for oral administration". In contrast, Applicants assert that the cited reference fails to disclose a drug comprising a 2-imidazolyl disulfide and an acceptable carrier for intravenous or oral administration. At best, Applicants submit that Oblong discloses a 2-imidazolyl disulfide in DMSO; however, DMSO is not an acceptable carrier for intravenous or oral administration. Accordingly, Oblong, as evidenced by Ashburn, fails to anticipate the present claims.

These arguments have been carefully considered, but are not found persuasive.

In the instant case, the Examiner acknowledges and does not dispute Applicants contention that Oblong et al. discloses a 2-imidazolyl disulfide in DMSO. However, in contrast to Applicants statement, those of skill in the art recognize that DMSO is an acceptable carrier for intravenous or oral administration as evidenced by Chaplan et al. and Padmanaban et al.. Thus, while Applicants statement has been considered, the Examiner recognizes that this statement appears to be an opinion which is not supported by any factual evidence and is in contrast to the knowledge possessed by those of skill in the art with respect to DMSO as a carrier for intravenous and oral administration as evidenced by Chaplan et al. and Padmanaban et al.

New Rejections Necessitated by Applicants Amendments:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

Independent claims 7 and 8 have been amended to recite the limitation "for intravenous administration". Applicants contend that support for this amendment can be found throughout the specification, including for example, paragraphs [0131] and [0215]. However, specification and claims, as originally filed, as well as the amendment to the specification submitted on 5/22/2008 (text search for intravenous), does not appear to lend support for the limitation "for intravenous administration". For example, paragraph [0131] recites the following:

> "Agents that inhibit thioredoxin have been identified in accordance with the present invention, such agents may be antibodies, drugs or antisense. A series of unsymmetrical 2-imidazolyl disulfides were investigated as inhibitors of the thioredoxin system and as potential anti tumor agents. Although these agents were originally identified as competitive inhibitors of thioredoxin reductase (Oblong J E, et al., Cancer Chemother. Pharmacol, 34:434-438, 1994) but it has now been shown that they also to bind irreversibly to Cys.sup.73 of thioredoxin and to block its reduction by thioredoxin reductase. A number of these disulfide compounds have been studied and have demonstrated anti-tumor activity against human tumor xenografts in Scid mice with up to 90% inhibition of MCF-7 breast cancer and HL-60 promyelocytic leukemia growth. It has now been demonstrated that the imidazolyl disulfides inhibit thioredoxin-dependent cell growth (Oblong J E, et al., Cancer Chemother. Pharmacol., 34:434-438, 1994) and that their growth inhibitory activity in the National Cancer Institute 60 human tumor cell line panel correlates with levels of thioredoxin mRNA in these cell lines (Berggren M, et al., Anticancer Res., 16:3459-3466, 1996). A COMPARE correlative analysis of the activity of the lead disulfide compounds in the NCI cell line panel with over 50,000 compounds already tested for cell growth inhibition by the NCI was conducted in order to identify compounds with a similar pattern of growth inhibitory activity: Some of the compounds identified in this way were inhibitor of thioredoxin reductase and some were inhibitors of thioredoxin."

Thus, this section appears to be silent on intravenous administration. Similarly, paragraph [0215] amended 5/22/2008 to incorporate subject matter taught in Powis, G., et al. Anticancer Drugs, 7 (suppl. 3): 121-126, 1996) recites the following:

> "The results of this study and our previous work (Gallegos, A. et al., Cancer Res., 56:5765-5770, 1996) suggest that the Trx system offers a novel target for agents to promote apoptosis and inhibit tumor growth, as well as to reverse the drug resistaice of some cancers. It is interesting, therefore, that some 2-imidazolyl disulfide inhibitors of Trx (Kuperus, M. et al., Proc. Am. Assoc. Cancer Res., 36:426, 1995) have been shown to induce apoptosis in cancer cells (Powis, G. et al., Anticancer Drugs, 7 (Suppl. 3):121126, 1996) and, in animal studies by intraperitoneal and oral administration, to have antitumor effects (Powis, G. et al., Anticancer Drugs, 7 (Suppl. 3):121-126, 1996).
> Hence, while this section provides support for oral administration and intraperitoneal

administration, it appears to be silent on the limitation of intravenous administration. Applicant is required to cancel the new matter in the response to this Office Action. Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above. See MPEP 714.02 and 2163.06.

Therefore, NO claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRANDON J. FETTEROLF whose telephone number is (571)272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf
Primary Examiner
Art Unit 1642

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